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Department of Bacteriology.

27 October, 1952.

Dear Luca,

Thanks for your letter and the photographs. Most of them, especially the group ones taken outside the Institute, are not very good but the one including Pupa and Nora on the boat to Stresa is excellent and we are very glad to have it. I am ashamed to say that I have not yet despatched the toy motors. As I told you, I bought a couple that were not so good and promised to send them off. I then got two more of the better variety and they have been sitting on my desk at home ever since. I have been very busy and kept saying to myself that I would pack them at the week-end and something seemed to happen and I put it off again! However, I promise most definitely to get them off this week. Anyway, the later the children receive them the longer they will have them!

Watson told me of his scheme and has now forwarded to me a copy of your analysis of it and I am struggling with this. My progress in genetics (classical) since I last saw you may be judged from the fact that I can follow most of it! It seems to me a clever concept and it appears to fit the facts in general, though it does not seem to have any great advantage over your view (which was also mine, based on a somewhat more naive foundation) that it is a part of a single F+ chromosome which is involved. I, of course, assumed that there was only one chromosome because the pundits had said so, but I am interested to hear that you have genetic evidence that, if this is really so, a break always seems to occur in the same place. Could it be that the F+ agent is an aberrant centromere which sometimes behaves in a "free-living" way, sometimes carries that part of the chromosome on one side of it as a kind of "tail", sometimes that part of the chromosome on the other side of it, and rarely the whole chromosome? This could account for your Hfr findings if one supposed that in these strains the F+ "centromere" was rarely, if at all, "free" and behaved in a reasonable fashion, as well as for my evidence (which, I admit, is only suggestive) that the F+ agent can occasionally act as a genetic carrier. This, at best, is wild speculation and probably nonsense, but I think you will admit that the whole business leaves plenty of room for speculation. As regards Jim's two chromosomes, he now seems to think that BM should be on chromosome B. This would seem to account for the evidence of linkage

between BM & B₁ in Lederberg's 1947 paper in which the method of reversed crosses, which might be invalidated by F, was not used. I am rather interested in trying a "ménage à trois" experiment (suggested by Watson) using one F- and two F+ strains, to see if the F- parent can acquire A & B from different ~~the~~ F+ parents. The difficulty about this kind of experiment is the existence of F+ transformations of the F- parent and F- phenocopies (or whatever they are) in F+ clones, but I think this can be got over by making pure F+ parents by SM-treatment. I have succeeded in convincing myself that the only fertile mating is F+ X F-.

If Watson's hypothesis appears to fit the facts well I certainly think that you and he should publish it jointly, but I cannot see any possible reason for my name being associated with it and would, I think, prefer to have it omitted.

About the C, L & L paper. Unfortunately I have no copy of the paper. Due to the rush about it prior to coming to Pallanza I only had two duplicate copies made (one of which went to the editor) + the original typescript which I did myself. If Joshua is not going to correct the proofs, could he send back his copy (he could have a copy made for himself) and you could then indicate to me on this copy what proof alterations you wanted? I see no reason for you to feel embarrassed at using the symbol "F" in the paper, no matter what the final interpretation of the nature of this factor turns out to be. I think it would be very confusing to call it ϕ unless this alteration is also made in the L, C & L paper in Genetics. Moreover, " ϕ " is usually used to indicate phage and there is no real evidence yet that F is a phage (though I think this very probable). My own feeling (anyway so far as my own paper is concerned) is that it would be better to leave things as they are as properly representing our views at the time the papers were submitted. If, then, you should obtain definite evidence that there is a locus for the maintenance of F according to the kappa or lambda models, the nomenclature can be changed. I cannot see that there is any very definite indication for change at the moment or, that, should things turn out as you anticipate from the F+ F- 1:1 segregations with your interesting uninfected F- strain, you need worry that you did not foresee this and incorporate it in a paper written a considerable time before. Of course, if you and Joshua decide it should be changed that is quite alright but I think you should then give reasons for the alteration in terminology. I think, however, I will let "F" stand in my own effort.

"Streptomycinase" — I rung up Lightbown about this this morning. This enzyme is produced by *Ps. pyocyanea* but, I fear, has no practical value. It is highly insoluble so that large volumes must be used to neutralise even quite small concentrations of SM. Moreover, it is itself quite markedly bacteriostatic and, again, will not reverse ~~the~~ the action of SM which has already been in contact with cells. It is really only a laboratory curiosity. Lederberg was interested in it but Lightbown considered it would be of no value to him either.

I am only just getting down to some bench work again, having done nothing for over two months. I will let you know anything interesting that turns up. Best wishes to Pupa from Nora and myself.

Yours ever,

Bill